Resgistration and prevention of congenital anomalies.

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Chapter 7: SUMMARY

As the relative contribution of congenital anomalies to infant mortality and morbidity increases, insight into their etiology becomes more and more important. A decrease of the prevalence of these anomalies is of major importance, as was stated in the WHO programme "Health for all by the year 2000". At present, in about 80% of cases the etiology of congenital anomalies is either multifactorial or unknown (Chapter 1). When the etiology of an anomaly is multifactorial, the individual genetic and environmental factors involved are unknown in almost all cases. In 1974 the Committee of Medical and Public Health Research of the European Community (EC) decided to set up a network of registrations of congenital anomalies in EC member states to increase the knowledge of the occurrence of congenital anomalies. This network was called EUROCAT: EUropean Registration Of Congenital Anomalies. In 1991 this network consisted of a total of 24 regional registrations in 13 countries, covering more than 380,000 births annually, with a central facility for coordination and research in Brussels (Chapter 2.2).

REGISTRATION OF CONGENITAL ANOMALIES

The first Dutch registration of congenital anomalies started in 1981 in the northern Netherlands. In the beginning an important question was whether such a registration would be feasable in the Netherlands. It turned out that many doctors, midwives and parents in the northern Netherlands were willing to collaborate in order to collect data on infants and fetuses with congenital anomalies (Chapter 2.2). Adequate protection of privacy could be achieved.

THE OCCURRENCE OF CONGENITAL ANOMALIES

The occurrence of congenital anomalies in one of the EUROCAT-regions, the northern Netherlands, is described in chapter 3. The measures of occurrence used are the livebirth prevalence, the total birth prevalence and the prevalence among live and stillbirths (Chapter 2.1). A total of 1251 children and fetuses born in the period 1981-1986 were notified to EUROCAT, which was 2.5% of all live and stillbirths covered (Chapter 3.1). In the northern Netherlands the total birth prevalence of neural tube defects (1.43 per 1000) is lower than in the United Kingdom (UK) and Ireland but higher than in other continental European regions. Cleft lip with or without palate (CLP), not combined with other malformations, also shows a high frequency (1.22 per 1000 births). This prevalence has been stable since 1970. The pattern of occurrence of CLP (e.g. sexratio, site of the defect) is similar to other regions (Chapter 3.2). Research on the reasons for the high prevalence is still being carried out.

ETIOLOGY OF CONGENITAL ANOMALIES

After the epidemic of limb reduction defects caused by thalidomide, it was hoped that any new epidemic of congenital anomalies would be detected at an earlier stage. Statistical monitoring techniques developed for this purpose were focussing on the birth prevalence in consecutive periods of time. Monitoring can be more sensitive by investigating combinations of potential risk factors and outcomes (Chapter 4.1). Using this new monitoring technique we found an association between ovulation stimulation and fetal neural tube defects (NTD) (Chapter 4.2).

DECREASING THE LIVEBIRTH PREVALENCE OF CONGENITAL ANOMALIES

When the etiology of a congenital anomaly is known, primary prevention may be possible. Rubella vaccination to prevent congenital rubella syndrome is a well-known example. Often the etiology of congenital anomalies is unknown, and the only way to avoid the livebirth of a child with a serious congenital anomaly is the termination of a pregnancy (TOP) after prenatal diagnosis of the anomaly.
In the Netherlands the prevention and intervention policy for congenital anomalies is mainly aimed at parents with a known increased risk. However, most children with congenital anomalies are born to parents who were not known to have an increased risk (Chapter 5.1). Therefore the present policy will not lead to a major further decline of the birth prevalence of congenital anomalies.
Chapters 5.2 and 5.3 concern prevention and intervention policies regarding chromosomal anomalies, chapter 5.4 concerns neural tube defects.
Prenatal cytogenetic diagnosis (PCD) in most EC countries is offered to pregnant women of advanced maternal age, to parents who have a history of a previous child with a chromosomal anomaly, to parents who are carriers of a balanced translocation, to mothers who are carriers of an X-linked disorder and to pregnant women in whom a fetal anomaly was detected at ultrasound (Chapter 5.2). In some EC countries there are additional indications. The exact maternal age limit varies from 35+ to 38+ years of age. In the last few years the PCD policy has been changing in some countries, especially in the UK and Switzerland, as individual risk calculation based on maternal serum markers became available and was improved. Individual risk assessment using maternal serum markers has the advantage that the number of Down syndrome cases diagnosed prenatally may increase, while the number of invasive procedures, such as amniocentesis (AC) and chorionic villi sampling (CVS), may decrease, even if we take into account an additional 1% of invasive procedures because of an increased NTD risk. With a decrease of invasive procedures, the number of iatrogenic abortions due to AC or CVS will also decrease.
The potential impact of PCD and termination of affected pregnancies in older mothers has been calculated in chapter 5.3. Data from nine EC countries was

used. Of live and stillbirths with serious chromosomal anomalies the percentage born to mothers older than 35 years of age in 1979-1982 varied from 19 in Belgium to 48 in Ireland. For the nine EC countries collaborating in this study it was estimated that 29% of children with unbalanced autosomal anomalies were born to mothers older than 35 years of age.
The total birth prevalence of NTD in Europe showed major regional differences: in the British Isles it varied from 24 to 38 per 10,000, in continental Europe from 10.7 to 14.3 per 10,000 (Chapter 5.4). This last figure represents the northern Netherlands. The impact of prenatal diagnosis and termination of affected pregnancies varied as well. In Ireland and Malta TOP was not available. In the other countries the percentage of anencephaly cases born at induced abortion varied from 47.4 in the northern Netherlands to 94.1 in Strasbourg. For spina bifida these figures varied from 2.7 in Northern Ireland to 52.9 in Glasgow. Early TOP was more common in British regions with serum alfa fetoprotein screening programs. TOP after 28 weeks of pregnancy was relatively common in France.

FUTURE DEVELOPMENTS: DOWN SYNDROME

It is hard to predict future developments regarding the birth prevalence of congenital anomalies. For Down syndrome, the total birth prevalence can be predicted from the developments in demographic factors (increasing age specific fertility in women aged 29+, increasing number of women aged 35+). The prevalence of Down syndrome conceptusses will increase as a result of demographic changes. Meanwhile the increased use of PCD will lead to a decrease of Down syndrome among livebirths. In chapter 5.6 a model is described to quantify the result of these changes on the Down syndrome prevalence. In the Netherlands, with present indications for PCD and with a utilization ratio of 50%, an increase of the livebirth prevalence of Down syndrome from 1.36 per 1000 in 1992 to 1.76 per 1000 in 2001 is to be expected. The number of PCD corresponding to these figures increases from 7,900 in 1992 to 14,500 in 2001. The number of iatrogenic abortions, caused by amniocentesis/ chorionic villi sampling, would increase from 79 to 145 annually. The model described in chapter 5.6 can be used to evaluate the consequences of alternative forms of Down syndrome screening.

FUTURE DEVELOPMENTS: GENERAL

Continued research has, in the past decade, led to the identification of factors associated with the origin of congenital anomalies (Chapter 6). Some of these factors have opened possibilities for primary prevention in the future. Research may reveal new risk factors. Strategies that are presently being used in other EC member states may inspire the Dutch health authorities to review the national prevention and intervention policy.

INFORMATION OF THE PUBLIC

Information available to scientists or health workers on the causes of congenital anomalies and on the possibilities to decrease the risks of congenital anomalies may not always reach the couples who plan to get pregnant. Some causes of congenital anomalies may not be identified and information on preventive or interventive options may not be passed on. When parents have a child with a serious congenital anomaly, referral for genetic counseling is a step to optimize the information on the etiology of their childs anomaly, the recurrence risk and possibilities for prevention and intervention. We compared the data of the northern Netherlands registration of congenital anomalies (years of birth 1981-1986) and data of the genetic clinic (Chapter 5.5). After the birth of the child with a congenital anomaly, 17% of the parental couples had been referred for genetic counseling. Some of the couples who do not use interventive policies (Chapter 5.2 and 5.3) may not be aware of these possibilities. Continued attention is needed to optimize the availability of information for future parents.